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PATENT

Attorney Docket 040750-5001-01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **H-J. Su Huang *et al.***

Application No. **09/071,541**

Filed: **May 4, 1998**

For: **Methods to Modulate the Resistance of Cells to Apoptosis Mediated by Mutant Epidermal Growth Factor Receptors**

Group Art Unit: **1623**

Examiner: **K. Fonda, Ph.D.**

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DECLARATION UNDER 37 C.F.R. 1.132

I, Webster K. Cavenee declare as follows:

1. I am a Director at the Ludwig Institute for Cancer Research and a Professor at University of California-San Diego. A copy of my Curriculum Vitae is attached as Exhibit A.

2. I am a named co-inventor of the above identified U.S. Patent Application 09/071,541.

3. The invention disclosed and claimed in U.S. Patent Application 09/071,541 is directed to methods of modulating an apoptosis-inhibiting effect in a target cell or tissue of a mutant EGFR gene comprising administering to the cell or tissue and effective amount of a tyrosine kinase inhibitor in combination with a therapy to induce apoptosis.

4. The claimed invention is a result of the collaborative effort of named inventors H-J. Su Huang, Motoo Nagane, Webster K. Cavenee, Alexander Levitzki and Aviv Gazit.

5. I am a named co-author of the abstract entitled "A tumor-specific mutant epidermal growth factor receptor confers cisplatin resistance in human glioblastoma cells by modulating Bcl-XL and caspase-3" which describes a presentation made at an American Association of Cancer Research (AACR) Special Conference held January 9 to 13, 1998 (Exhibit B). This abstract mentioned the testing of CDDP treatment of 087MG.ΔEGFR cells in combination with tyrphostins as a matter under investigation at the time the abstract was submitted.

6. While the published abstract of the presentation made at the AACR Special Conference omits Alexander Levitzki and Aviv Gazit as authors, the testing mentioned in the last line of the

abstract, was in fact a result of a collaborative effort between H-J. Su Huang, Motoo Nagane, Webster K. Cavenee, Alexander Levitzki and Aviv Gazit. To the extent that the abstract teaches a concept claimed in this application, the authors of the published abstract derived their knowledge of such concept from the combined inventive entity.

7. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

Webster K. Cavenee, Ph.D.

3/3/03
Date

Exhibit A

Curriculum Vitae:

Webster K. CAVENEE

Webster K. Cavenee
Director, Ludwig Institute for Cancer Research
(San Diego Branch)
Professor, University of California-San Diego

Address:	Ludwig Institute for Cancer Research 9500 Gilman Drive La Jolla, CA 92093-0660 Tel: (858) 534-7802 FAX: (858) 534-7750 E-mail: wcavenee@ucsd.edu
Date and Place of Birth:	12 September 1951, Manhattan, Kansas
Nationality:	USA
Marital Status:	Married, two children
Experience:	
1991-Present	Director, Ludwig Institute for Cancer Research (San Diego Branch) Professor, Department of Medicine, UCSD Member, Center for Molecular Genetics, UCSD Member, Cancer Center, UCSD
1986-1991	Director, Ludwig Institute for Cancer Research (Montreal Branch) Associate then full Professor, Departments of Medicine, Neurology, Pathology and Human Genetics McGill University, Montreal
1983-1986	Assistant then Associate Professor Department of Microbiology and Molecular Genetics University of Cincinnati
1981-1983	Associate Howard Hughes Medical Institute University of Utah Medical School
1979-1981	Visiting Research Scientist Center for Cancer Research Massachusetts Institute of Technology

1977-1979	Postdoctoral Fellow The Jackson Laboratory
1973-1977	NIH Predoctoral Fellow (Ph.D.) Department of Microbiology University of Kansas Medical School
1969-1973	Undergraduate (B.Sc.) Department of Biology Kansas State University

Honors and Awards:

A) Prizes and Awards

1977	Ph.D. Awarded with Distinction.
1978-1979	Anna Fuller Fund Postdoctoral Fellowship.
1979-1982	National Research Service Award, NCI, NIH.
1983	Basil O'Connor Award, March of Dimes Birth Defects Foundation.
1988	Rhoads Prize, American Association for Cancer Research.
1989	Esther Langer Award, University of Chicago.
1990	Charles S. Mott Award, General Motors Cancer Research Foundation, New York.
1994	Farber Prize, American Association of Neurological Surgeons.
2002	DS.c. (Honoris Causis), University of Cincinnati.
2002	Anthony Dipple Senior Carcinogenesis Award, European Association for Cancer Research, Granada, Spain.
2002	Raymond Bourgine Award, Paris, France.

B) Plenary and Named Lectures

1985	International Union Against Cancer (UICC) Visiting Professor, Karolinska Institute, Stockholm, Sweden.
1987	Fullbright Lectures, University of Siena Medical School, Siena, Italy.
1987-1991	Fellow, The Environmental Health Institute.
1988	Sokolow Visiting Professor, University of California, San Francisco.
1988	Steele Visiting Professor, Memorial-Sloan Kettering Cancer Center, New York.
1989	Menten Memorial Lecture, University of Pittsburgh.

1989 Dean's Lecture, University of Colorado, Denver.

1989 Graduate Lecture, University of Cincinnati.

1989 Giblin Memorial Lecture, Columbia College of Physicians and Surgeons.

1989 Keynote Lecture, European Society for Human Genetics, Groningen, The Netherlands.

1989 Fishman-Moore Distinguished Lecture, American Association of Neuropathologists, Dallas, Texas.

1989 Jenkinson Memorial Lecture, University of Oxford.

1990 Trimble Lecture, University of Tennessee.

1991 Plenary Lecture, International Society of Pediatrics, Rhodes, Greece.

1992 Louis Channing Ball Lecture, University of Southern California, Los Angeles.

1992 American Cancer Society Distinguished Lecture, University of Kentucky, Lexington.

1992 Plenary Lecture, International Symposium on Genetic Eye Disease, Siena, Italy.

1992 Distinguished Lecture, University of California, Los Angeles.

1992 American Cancer Society Distinguished Lecture, Norfolk, Virginia.

1992 Art Stern Lecture, Wistar Institute, Philadelphia, Pennsylvania.

1993 Ben Abelson Lecture, Washington University, St. Louis, Missouri.

1993 Distinguished Faculty Lecture, University of California, San Diego.

1993 Keynote Lecture, American Society of Radiological Oncology, New Orleans, Louisiana.

1993 University Distinguished Lecture, Southwestern Medical School, Dallas, Texas.

1993 Corpus Ortegoza Lecture, Baylor College of Medicine, Houston, Texas.

1993 Distinguished Lecture, University of Kansas Medical School, Kansas City.

1994 Decade of the Brain Distinguished Lecture, Loyola Stritch School of Medicine, Chicago.

1994 Distinguished Lecture, University of Pittsburgh Cancer Center.

1994 Plenary Lecture, AACR Conference on Translational Research, Asheville, North Carolina.

1995 Bugher Foundation Lecture, University of California-San Diego.

1995 Swerling Lecture, Dana Farber Cancer Institute, Harvard Medical School.

1995 Plenary Lecture, 16th Congress of the Italian Society for Histochemistry, Naples.

1995 Plenary Lecture, Italian Society of Pediatric Oncology, Bari.

1995 Weinhouse Lecture, Jefferson Cancer Institute, Philadelphia.

1996 Hamilton Fairley Lecture, Royal Society of Medicine, London.

1996 Plenary Lecture, Joint Session of the Hong Kong International Cancer Conference and the Epstein-Barr Virus Symposium, Hong Kong.

1996 Plenary Lecture, 13th Asia Pacific Cancer Conference, Penang, Malaysia.

1997 Plenary Lecture, Beatson Cancer Conference, Glasgow, Scotland.

1998 Horizons in Biomedical Research Lecture, Lerner Research Institute, Cleveland.

1998 Donald S. Coffey Lecture, American Association of Urologic Surgeons, San Diego.

1998 Plenary Lecture, The Pathological Society, Leicester, England.

1999 The Deborah M. Richman Lectureship, the University of Texas MD Anderson Cancer Center, Houston.

1999 Plenary Lecture, San Antonio Symposium on Biomedical Sciences, San Antonio, TX.

1999 Plenary Lecture, International Society of Neuro-oncology, Scottsdale, AZ.

1999 Plenary Lecture, Japan Cancer Association, Hiroshima, Japan.

1999 Distinguished Lecture, Chinese University of Hong Kong.

1999 Plenary Lecture, Japan Neurosurgical Society, Tokyo.

2000 Keynote Address, University of Chicago, First Joint Meeting of the Committee on Cancer Biology and the Committee on Human Nutritional Biology.

2000 The Eighth Annual Melvin L. Samuels Lectureship, The University of Texas MD Anderson Cancer Center, Houston, Texas.

2000 Special Lecture, Second International Symposium of Brain Tumor Pathology, Nagoya, Japan.

2000 Robert W. Owen Lecture, London Regional Cancer Center, University of Western Ontario, Canada.

2000 Honors Lecture, New York University Medical School, New York.

2000 Distinguished Lecture, Roswell Park Cancer Institute, Buffalo, NY.

2000 Plenary Lecture, FECS/AACR/ASCO Workshop on "Methods in Clinical Cancer Research", Flims, Switzerland.

2001 Keynote Lecture, University of California-Irvine, Basic Cancer Research Forum.

2001 Keynote Lecture, University of Oregon Health Sciences Center, Graduate Student Research Forum.

2001 Brain Tumor Society Lecture, 14th International Brain Tumor Conference, Asheville, NC.

2002 Charles Wilson Lecture, University of California-San Francisco.

2002 Distinguished Lecture, Fox-Chase Cancer Center.

2002 Principal Lecture, Hiroshima Cancer Symposium.

2002 Distinguished Lecture, Duke University Medical School, NC.

2002 Distinguished Lecture, Washington University School of Medicine.

2002 Plenary Lecture, International Conference on Translational Cancer Research and Therapy, Tianjin, China.

2002 Plenary Lecture, Medicine in the 21st Century, Second Sino-US Symposium, Shanghai, China.

2003 Balkin Lecture, Massachusetts General Hospital, Boston, MA.

Professional Societies:

American Society for Human Genetics.
American Society for Microbiology.
American Association for the Advancement of Science.
American Association for Cancer Research.
International Union Against Cancer (elected Fellow, 1994).
American Society of Clinical Investigation (elected Honorary Member, 1995).
American Academy of Microbiology (elected Fellow, 1997).
National Academy of Sciences (elected Member, 1997).
Joint Section on Tumors, American Association of Neurological Surgeons and Congress of Neurological Surgeons (elected Honorary Member, 2002).

Scientific Committees:

A) Advisory Boards/Boards of Directors

1985	NCI Advisory Group on Procurement of Tumor Tissues.
1986	Discussant, President's Cancer Panel, Memphis.
1986	Consulting Board of American Type Culture Collection.
1987-1990	Curator, American Type Culture Collection Human DNA Probe Repository.
1988-1992	Founding Council, Human Genome Organization.
1988-1992	Scientific Advisory Board, GeneScreen, Inc., Dallas.
1989-1993	Member, Scientific Advisory Board, Damon Runyon - Walter Winchell Cancer Fund.
1989-1994	Board of Scientific Counselors, Division of Cancer Etiology, NCI.
1990-1996	Scientific Advisory Board, Raggio-Italgene, Sp.A., Rome.
1991-1997	Scientific Advisory Board, Somatix, Alameda, CA.
1991-2000	Board of Directors, UCSD Cancer Center, San Diego.
1991-	Scientific Advisory Board, Robert Steel Foundation for Pediatric Cancer Research, New York.
1992-1995	Scientific Committee, International Society of Preventive Oncology.
1993-1996	Scientific Advisory Board, Bristol Myers-Squibb Oncology Division, Princeton.
1993-1996	Consultant, Specialty Labs, Santa Monica.
1993-1997	Foundation and Steering Committee, International Society of Tumour Targeting.
1994-2001	Advisory Board, Norris Cancer Center, University of Southern California.
1994-1996	Scientific Advisory Board, National Neurofibromatosis Foundation.
1994-1997	Board of Directors, American Association for Cancer Research.
1994-	Scientific Advisory Board, Aspen Cancer Conference.
1995-2001	Board of Directors, Damon Runyon-Walter Winchell Cancer Research Fund.
1995-	Advisory Council, American Brain Tumor Association.
1995-2001	Advisory Committee, University of Minnesota Cancer Center, Minneapolis.
1996-2001	Advisory Committee, University of Michigan Cancer Center, Ann Arbor.

1996-1999	Board of Scientific Counselors, National Institute of Environmental Health Sciences, NIH.
1996-	Scientific Advisory Board, Kimmel Cancer Foundation.
1997-	Scientific Advisory Council, The Brain Tumor Society.
1997-2001	Scientific Advisory Board, The Guy Forbeck Foundation for Pediatric Research.
1997-1998	Scientific Advisory Board, Boehringer-Mannheim GmBH, Tutsing, Germany.
1997-	Scientific Advisory Board, Kimmel Cancer Center, San Diego, CA.
1997-1998	Scientific Advisory Board, GenQuest, Inc., Seattle, WA.
1997	President-Elect, American Association for Cancer Research.
1998	President, American Association for Cancer Research.
1998-	Scientific Advisory Board, Angstrom Pharmaceuticals, San Diego, CA.
1998-	Board of Directors, Dnaform, K. K., Tsukuba, Japan.
1999	Past President, American Association for Cancer Research.
1998-2001	Scientific Advisory Board, Lerner Research Institute, The Cleveland Clinic Foundation.
1998-2003	Chair, Scientific Advisory Board, The McDonnell Foundation Brain Tumor Program.
1999-2001	Scientific Advisory Board, The Van Andel Institute for Biomedical Research, Grand Rapids, MI.
2000-	Scientific Advisory Board, People's Genetics, Inc., Boston, MA.
2000-	Scientific Advisory Board, Attenuon, L.L.C., San Diego, CA.
2001-	Scientific Advisory Board, University of Kansas Medical School.
2002-	Scientific Advisory Committee, International Cancer Center, Rovigo, Italy.
2002-	Scientific Advisory Board, Five Prime Therapeutics, Inc., San Francisco, CA.
2002-	Scientific Advisory Board, Center for Environmental Health Sciences, MIT, Cambridge, MA.
2002-	Scientific Advisory Committee, Duke University Comprehensive Cancer Center.
2002-	Chair, Scientific Advisory Board, University of California at San Francisco Brain Tumor Program.
2002-	Chair, Executive Committee, World Alliance of Cancer Research Organizations.

B) Grants/Program Review Boards

1985	NCI Special Study Section on Application of Recombinant DNA Technology to the Diagnosis of Cancer.
1986	Ad hoc member Mammalian Genetics Study Section, NIH.
1986	NCI Special Study Section on Inheritance and Markers of Colorectal Cancer and Polyps.
1986-	Ad hoc Reviewer for Medical Research Council (Canada), National Cancer Institute (Canada), and the Alberta Heritage Foundation for Medical Research.
1987	Reviewer, Laboratory of Viral Carcinogenesis, NCI.
1988	Reviewer, Laboratory of Cellular and Molecular Biology, NCI.
1988	NCI Special Review Committee on National Cooperative Drug Discovery Groups.
1989-1990	Molecular Biology Review Panel (F), National Cancer Institute of Canada.
1990	Reviewer, Laboratory of Molecular Oncology, NCI.
1991	Reviewer, Laboratory of Tumor Virus Biology, NCI.
1992	Reviewer, M.D. Anderson Cancer Center Core Grant.
1992	Reviewer, Cancer Research Campaign Unit, Sutton, UK.
1993	Chair, Review Team, Laboratory of Molecular Virology, NCI.
1993	Chair, Review Team, Laboratory of Virus Biology, NCI.
1993	Reviewer, Imperial Cancer Research Fund, London UK.
1993	Reviewer, Cancer Research Campaign Units, Cambridge and Manchester, UK.
1993	NCI Panel on Genetic Epidemiology.
1994	Review Committee, Cancer Programs, University of Wisconsin.
1994	Chair, Review Team, Laboratory of Cellular and Molecular Biology, NCI.
1995	Chair, Site Visit Team, University of Arizona Cancer Center.
1995	Chair, Review Team, Program on "Cell Differentiation and Carcinogenesis", DKFZ, Heidelberg.
1996	Reviewer, Laboratory of Human Carcinogenesis, NCI.
1997	Reviewer, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.
1998	Reviewer, Laboratory of Toxicology, NIEHS.

1999	Reviewer, Swiss National Cancer Program.
1999	Reviewer, Laboratory of Structural Biology, NIEHS.
1999	Reviewer, Laboratory of Molecular Genetics, NIEHS.
2000	Program Review Group, Brain Tumors, NINDS and NCI.
2000	Reviewer, Genetics Program, Cleveland Clinic.
2001	Review Panel, RIKEN Genome Sciences Center, Yokohama, Japan.
2000-2002	Reviewer, Various Units, Cancer UK, Cambridge, Sutton, Glasgow.

C) Meeting Organization

1989	Co-chair, Banbury Conference on Recessive Oncogenes.
1989	Co-chair, Gordon Conference on Cancer.
1990	Chair, Gordon Conference on Cancer.
1991	Organizer, AACR Symposium on Development and Childhood Malignancies.
1991	Organizer, ACS National Conference on Integration of Molecular Genetics into Cancer Management.
1991	Chair, Program Committee 1992 Annual Meeting, American Association for Cancer Research.
1992	Chair, NCI Symposium on Genetic Epidemiology.
1992	Chair, NCI Symposium on p53 in Cancer.
1992	Organizer, AACR Conference on Genetics and Cancer.
1993	Organizer, Annual Meeting on Oncogenes, Frederick, Maryland.
1993	Chair, NCI Symposium on Helicobacter and Gastric Cancer.
1994	Organizer, NCI Symposium on Cancer Genetics and Population Screening.
1995	Co-organizer, Symposium on "Molecular Detection and Prevention of Cancer", NIH, Bethesda, MD.
1996	Co-organizer, International Symposium of the Foundation for Promotion of Cancer Research, Tokyo.
1997	Co-organizer, AACR/LCC Meeting on Growth Factors and Cancer, Lorne, Australia.
1997	Co-organizer, AACR/Joint Section Meeting on Cancer of the Central Nervous System, Coronado, California.
1997-2000	Co-organizer, Usha Mahajani Symposium, UCSD and Salk Institute, La Jolla, California.

1999	Organizer, International Summit of Cancer Association Leaders, Bangkok, Thailand.
2000	Organizer, "West Coast Vision for Genomics in the Post-Sequencing Era", Lawrence Berkeley National Laboratory, Berkeley, California.
2000	Chair, American Association for Cancer Research/Israel Cancer Association Conference on "New Targets for Cancer Intervention", Eilat, Israel (postponed due to conflict).
2001	Chair, American Association for Cancer Research/Japan Cancer Research Conference on "Molecular Biology and New Therapeutic Strategies: Cancer Research in the 21st Century", Maui, Hawaii.
2002	Chair, Preuss Symposium on "Novel Therapies for Brain Cancer", San Diego, CA.
2002	Co-organizer, 12th International Symposium of the Hiroshima Cancer Seminar, Hiroshima, Japan.
2003	Chair, Goldhirsh-McDonnell Symposium on "New Concepts and Treatments for Tumors of the Central Nervous System", Lago Como, Italy.

D) Prize Selection Committees

1989	Selection Committee, Clowes Award, American Association for Cancer Research.
1991	Selection Committee, Mott Award, General Motors Cancer Research Foundation.
1992	Chair, Mott Award Selection Committee, General Motors Cancer Research Foundation.
1994-1998	Assembly, General Motors Cancer Research Foundation.
1995	Chair, Clowes Award, Selection Committee, AACR.
2001	Rosenthal Award Selection Committee, AACR.
2002	Clowes Award Selection Committee, AACR.

Editorial Boards:

Permanent - Genomics, Cell Growth and Differentiation, Tumour Targeting, DNA and Cell Biology, Genetic Epidemiology and Cancer Prevention, International Journal of Cancer, Japanese Journal of Cancer Research, Neuro-Oncology.

Ad hoc - Nature, Science, Molecular and Cellular Biology, Journal of Biological Chemistry, Human Genetics, American Journal of Human Genetics, Somatic Cell and Molecular Genetics, Proceedings of the National Academy of Sciences U.S.A.

Past - Oncogene Research (1986-1991), Cytogenetics and Cell Genetics (1986-1991), Methods in Molecular Biology (1988-1993), Journal of Heredity (1991-1996), Journal of Clinical Investigation (1992-1997), Cancer Epidemiology, Biomarkers and Prevention (1996-2001), Journal of Clinical Investigation (Consulting Editor, 1998-2002), Genes Chromosomes and Cancer (1992-2002), Cancer Research (1987-2002).

Teaching:

Molecular genetics for graduate students (1983-2002).
Molecular genetics for medical students (1983-1986).
Bar Harbor course in experimental genetics (1985, 1986).
Cold Spring Harbor course in human neurobiology (1986, 1987).
NATO course in molecular oncology (1989, 1990, 1994, 1996).
Molecular pathology for medical students (1987-1991 - McGill; 1992 - UCSD).
Stanford University course in molecular oncology (1989, 1990, 1992, 1994, 1996).

Patents:

US 5,990,280 Glioblastoma-Derived Angiogenesis Inhibitory Factor.
Issued November 23, 1999.

US 6,444,640 Compositions of TRAIL and DNA-damaging Drugs and Uses Thereof
Issued September 3, 2002.

Trainees:

Marc Hansen	Graduate Student	(1983-1988)
Heidi Scrable	Graduate Student	(1984-1989)
Stephanie Glynn	Graduate Student	(1986-1990)
Tom Mikkelsen	Graduate Student	(1988-1992)
Wadih Arap	Graduate Student	(1993-1996)
Wendy Smith	Graduate Student	(2001-present)
Michelle Mendoza	Graduate Student	(2001-present)
Janet Buchanan	Postdoctoral Fellow	(1984-1987)
Alex Koufos	Postdoctoral Fellow	(1984-1988)
David James	Postdoctoral Fellow	(1986-1989)
Marie-Christine Guiot	Postdoctoral Fellow	(1986-1989)
Lois Mulligan	Postdoctoral Fellow	(1986-1990)
Karen Arden	Postdoctoral Fellow	(1987-1991)
Paul Grundy	Postdoctoral Fellow	(1987-1988)
David Foran	Postdoctoral Fellow	(1988-1990)
Irene Newsham	Postdoctoral Fellow	(1988-1991)
Patricia Tonin	Postdoctoral Fellow	(1989-1991)
Sandra Rempel	Postdoctoral Fellow	(1990-1992)
Jürgen Weiss	Postdoctoral Fellow	(1990-1993)
Dana Lasko	Postdoctoral Fellow	(1990-1991)
Adekunle Adesina	Postdoctoral Fellow	(1990-1991)
Jan Moreb	Postdoctoral Fellow	(1990-1991)
Erwin Van Meir	Postdoctoral Fellow	(1991-1994)
Corinne Besnard-Guerin	Postdoctoral Fellow	(1992-1994)
Vicki Chazin	Postdoctoral Fellow	(1992-1994)
Linda Wasserman	Postdoctoral Fellow	(1992-1995)
Oliver Bögler	Postdoctoral Fellow	(1994-1997)
Friedrich Finckenstein	Postdoctoral Fellow	(1994-1997)
Michael Harding	Postdoctoral Fellow	(1992-1997)
Michael Anderson	Postdoctoral Fellow	(1993-2000)
Andrea Kindler-Röhrborn	Postdoctoral Fellow	(1992-1994)
Ryo Nishikawa	Postdoctoral Fellow	(1992-1995)
Beth McLellan	Postdoctoral Fellow	(1992-1993)
Robert Winqvist	Postdoctoral Fellow	(1992-1994)

Frank Furnari	Postdoctoral Fellow	(1993-2000)
Rudolf Herbst	Postdoctoral Fellow	(1993-1995)
Shiyuan Cheng	Postdoctoral Fellow	(1993-1999)
Degui Wang	Postdoctoral Fellow	(1994-1999)
William Biggs	Postdoctoral Fellow	(1994-2002)
Joseph Costello	Postdoctoral Fellow	(1994-2000)
Motoo Nagane	Postdoctoral Fellow	(1995-1999)
Frank Coufal	Postdoctoral Fellow	(1995-1997)
Lukas Amler	Postdoctoral Fellow	(1996-1997)
Vivian Wei Wang	Postdoctoral Fellow	(1996-1997)
Karen Knudsen	Postdoctoral Fellow	(1997-1998)
Gavin Robertson	Postdoctoral Fellow	(1997-2001)
Erika Hatva	Postdoctoral Fellow	(1997-1999)
Kazuhiko Mishima	Postdoctoral Fellow	(1997-2001)
Charles de Smet	Postdoctoral Fellow	(1998-2000)
Hiroyuki Nishimori	Postdoctoral Fellow	(1998-2000)
Andreas Waha	Postdoctoral Fellow	(1999-2001)
Yen-Liang Chen	Postdoctoral Fellow	(1999-present)
Xiaoying Fu	Postdoctoral Fellow	(1999-2001)
Yoshitaka Narita	Postdoctoral Fellow	(1999-present)
Koichi Okumura	Postdoctoral Fellow	(2001-present)
Anna Al-Khouri	Postdoctoral Fellow	(2001-present)
Susanna Mac	Postdoctoral Fellow	(2001-2002)
Taisuke Hosaka	Postdoctoral Fellow	(2001-present)
Wen Lu	Postdoctoral Fellow	(2002-present)
Imre Berek	Visiting Professor, Szeged	(1986-1989)
Elisabeth Carlbom	Visiting Professor, Stockholm	(1988)
Hans Scheffer	Visiting Professor, Groningen	(1988)
Maria Aparecida	Visiting Professor, Sao Paulo	(1990)
Doris Hadjistilianou	Visiting Professor, Siena	(1990)
Domenico Mastrangelo	Visiting Professor, Siena	(1990)
Karl Schwechheimer	Visiting Professor, Freiberg	(1991-1993)

Publications:

(A) Research articles:

Cavenee WK and Melnykovych G. Induction of 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase in HeLa Cells by Glucocorticoids. Journal of Biological Chemistry 252: 3272-3276, 1977.

Cavenee WK, Johnston D and Melnykovych G. Regulation of Cholesterol Biosynthesis in HeLa S3G Cells by Serum Lipoproteins: Dexamethasone-Mediated Interference with Suppression of 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase. Proceedings of the National Academy of Sciences USA 75: 2103-2107, 1978.

Johnston D, **Cavenee WK**, Ramachandran CK and Melnykovych G. Cholesterol Biosynthesis in a Variety of Cultured Cells: Lack of Correlation Between Synthesis and Activity of 3-Hydroxy-3-Methyglutaryl Coenzyme A Reductase Caused by Dexamethasone. Biochemica Biophysica Acta 572: 188-192, 1979.

Cavenee WK and Melnykovych G. Elevation of HeLa Cell 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase Activity by Glucocorticoids: Possible Relationship to the Cell Cycle. Journal of Cellular Physiology 98: 199-212, 1979.

Chen HW, **Cavenee WK** and Kandutsch AA. Sterol Synthesis in Variant Chinese Hamster Lung Cells Selected for Resistance to 25-Hydroxycholesterol: Cross-Resistance to 7-Ketocholesterol, 20α-Hydroxycholesterol and Serum. Journal of Biological Chemistry 254: 715-720, 1979.

Cavenee WK, Gibbons GF, Chen HW and Kandutsch AA. Effects of Various Oxygenated Sterols on Cellular Sterol Biosynthesis in Chinese Hamster Lung Cells Resistant to 25-Hydroxycholesterol. Biochemica Biophysica Acta 575: 255-265, 1979.

Gibbons GF, Pullinger CR, Chen HW, **Cavenee WK** and Kandutsch AA. Regulation of Cholesterol Biosynthesis in Cultured Cells by Probable Natural Precursor Sterols. Journal of Biological Chemistry 255: 395-400, 1980.

Cavenee WK, Chen HW and Kandutsch AA. Cell-Substratum and Cell-Monolayer Adhesion Are Dependent upon Cellular Cholesterol Biosynthesis. Experimental Cell Research 131: 31-40, 1981.

Cavenee WK, Chen HW and Kandutsch AA. Regulation of Cholesterol Biosynthesis in Enucleated Cells. Journal of Biological Chemistry 256: 2675-2681, 1981.

Cavenee WK and Baker RM. Characterization of Dominant Hamster Cell Mutants Resistant to Oxygenated Sterols. Somatic Cell Genetics 8: 557-574, 1982.

Cavenee WK, Dryja TP, Phillips RA, Benedict WF, Godbout R, Gallie BL, Murphree AL, Strong LC and White RL. Expression of Recessive Alleles by Chromosomal Mechanisms in Retinoblastoma. Nature 305: 779-784, 1983.

Cavenee W, Leach R, Mohandas T, Pearson P and White R. Isolation and Regional Localization of DNA Segments Revealing Polymorphic Loci from Human Chromosome 13. American Journal of Human Genetics 36: 10-24, 1984.

Dryja TP, **Cavenee W,** White R, Rapoport JM, Peterson R, Albert DM and Bruns GAP. Homozygosity of Chromosome 13 in Retinoblastoma. New England Journal of Medicine 310: 550-553, 1984.

Koufos A, Hansen MF, Lampkin BC, Workman ML, Copeland NG, Jenkins NA and **Cavenee WK.** Loss of Alleles at Loci on Human Chromosome 11 During Genesis of Wilms' Tumour. Nature 309: 170-172, 1984.

Nordenskjöld M, **Cavenee WK,** Kumlin E and Kock E. Bärardiagnostik av Retinoblastom med Molekylärgenetiska Metoder. Läkartidningen 81: 1183-1192, 1984.

Nordenskjöld M, **Cavenee WK,** Kumlin E and Kock E. Retinoblastom en Nyupptäckt Mekanism för Uppkomst av Cancer. Läkartidningen 81: 1192-1194, 1984.

Cavenee WK, Hansen MF, Nordenskjold M, Kock E, Maumenee I, Squire JA, Phillips RA and Gallie BL. Genetic Origin of Mutations Predisposing to Retinoblastoma. Science 228: 501-503, 1985.

Koufos A, Hansen MF, Copeland NG, Jenkins NA, Lampkin BC and **Cavenee WK.** Loss of Heterozygosity in Three Embryonal Tumours Suggests a Common Pathogenetic Mechanism. Nature 316: 330-334, 1985.

Hansen MF, Koufos A, Gallie BL, Phillips RA, Fodstad Ø, Brøgger A, Gedde-Dahl T and **Cavenee WK.** Osteosarcoma and Retinoblastoma: A Shared Chromosomal Mechanism Revealing Recessive Predisposition. Proceedings of the National Academy of Sciences USA 82: 6216-6220, 1985.

Dryja TP, Rapaport JM, Epstein J, Goorin AM, Weichselbaum R, Koufos A and **Cavenee WK.** Chromosome 13 Homozygosity in Osteosarcoma without Retinoblastoma. American Journal of Human Genetics 38: 59-66, 1986.

Cavenee WK, Murphree AL, Shull MM, Benedict WF, Sparkes RS, Kock E and Nordenskjold M. Prediction of Familial Predisposition to Retinoblastoma. New England Journal of Medicine 314: 1201-1207, 1986.

Cavenee WK, Koufos A and Hansen MF. Recessive Mutant Genes Predisposing to Human Cancer. Mutation Research 168: 3-14, 1986.

Leppert M, **Cavenee W,** Callahan P, Holm T, O'Connell P, Thompson K, Lathrop GM, Lalouel J-M and White R. A Primary Genetic Map of Chromosome 13q. American Journal of Human Genetics 39: 425-437, 1986.

Cavenee WK. The Genetic Basis of Neoplasia: The Retinoblastoma Paradigm. Trends in Genetics, 2: 299-300, 1986.

Griffin CA, Emanuel BS, Hansen JR, **Cavenee WK** and Myers JC. Human Collagen Genes Encoding Basement Membrane α 1 (IV) and α 2 (IV) Chains Map to the Distal Long Arm of Chromosome 13. Proceedings of the National Academy of Sciences USA 84: 512-516, 1987.

Lundberg C, Skoog L, **Cavenee WK** and Nordenskjöld M. Loss of Heterozygosity in Human Ductal Breast Tumors Indicates a Recessive Mutation on Chromosome 13. Proceedings of the National Academy Sciences USA 84: 2372-2376, 1987.

Buchanan JA and **Cavenee WK**. Genetic Markers for Assessment of Retinoblastoma Predisposition. Disease Markers 5: 141-152, 1987.

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Cavenee WK. Genetics and New Approaches to Cancer Therapy. Carcinogenesis 23: 683-686, 2002.

Cavenee WK. Musculing in on Rhabdomyosarcoma. Nature Medicine 8: 1200-1201, 2002.

Bögler O and **Cavenee WK**. Methylation and Genomic Damage in Gliomas. In Genomic and Molecular Neuro-Oncology. G. Fuller and W. Zhang, eds. Jones and Bartlett Publishers, Inc., Sudbury, MA.

Invited Lectures:

July, 1982	Department of Human Genetics, Sylvius Laboratories, University of Leiden, Leiden, The Netherlands.
August, 1982	Institute of Molecular Pathology, University of Paris, France.
August, 1982	Division of Environmental Carcinogenesis, International Agency for Research on Cancer, World Health Organization, Lyon, France.
September, 1982	Symposium on Molecular Genetics, American Society of Human Genetics Meeting, Detroit, Michigan.
October, 1982	International Symposium on Retinoblastoma, Monterey, California.
July, 1983	FASEB Research Conference on Somatic Cell Genetics, Saxton's River, Vermont.
October, 1983	Department of Clinical Genetics, Karolinska Institute, Stockholm, Sweden.
January, 1984	Ontario Cancer Institute, University of Toronto, Toronto, Canada.
February, 1984	Division of Hematology/Oncology, Children's Hospital of LA, USC Medical School, Los Angeles, California.
February, 1984	Symposium on Molecular Genetics of the Retina, National Eye Institute, Washington, DC.
February, 1984	Department of Biological Chemistry, Wright State University, Dayton, Ohio.
April, 1984	Department of Microbiology, New Jersey College of Medicine and Dentistry, Newark, New Jersey.
June, 1984	Sylvius Laboratories, University of Leiden, Leiden, The Netherlands.
June, 1984	Boerhaave Symposium on The Application of Molecular Biological Methods for the Clinic, University of Leiden, Leiden, The Netherlands.
September, 1984	Department of Pathology, University of Minnesota Minneapolis, Minnesota.
October, 1984	Department of Biology, University of Dayton, Dayton, Ohio.
October, 1984	National Cancer Institute, Bethesda, Maryland.
December, 1984	Merck Sharp and Dohme Research Laboratories, West Point, Pennsylvania.
January, 1985	Somatic Cell Genetics Conference, San Diego, California.
February 1985	Symposium on Experimental Eye Pathology, National Eye Institute, Bethesda, Maryland.
March, 1985	Departments of Human Genetics and Therapeutic Radiology, Yale University Medical School, New Haven, Connecticut.
April, 1985	Symposium on Human Molecular Genetics, American Society of Biological Chemists, Anaheim, California.
May, 1985	Symposium on Pediatric Tumors, American Society of Clinical Oncologists, Houston, Texas.
May, 1985	Program in Human Genetics and Department of Biology, McGill University, Montreal, Canada.
June, 1985	Department of Medical Genetics, Mt. Sinai School of Medicine, New York, New York.
June, 1985	Symposium on Oncogenes and Chromosome Alterations International Conference on Environmental Mutagens, Stockholm, Sweden.
June, 1985	Department of Clinical Genetics, Karolinska Institute, Stockholm, Sweden.
July, 1985	Department of Tumor Biology, Karolinska Institute, Stockholm, Sweden.
August, 1985	FASEB Conference on Vision, Saxton's River, Vermont.
August, 1985	Gordon Conference on Cancer, New London.
September, 1985	General Motors Cancer Research Foundation Conference, Bar Harbor, Maine.
November, 1985	Maimonides Conference on Cancer Research, Ein Gedi Israel.
December, 1985	Institute for Cancer Research Fox-Chase Cancer Center, Philadelphia, Pennsylvania.
January, 1986	Department of Cell Biology and the Cancer Center University of New Mexico Medical School, Albuquerque, New Mexico.
January, 1986	Division of Medical Genetics, Department of Medicine, Henry Ford Hospital, Detroit, Michigan.

March, 1986	Departments of Experimental Therapeutics and Human Genetics, Roswell Park Memorial Institute.
March, 1986	Department of Human Genetics, University of Michigan Medical School, Ann Arbor, Michigan.
March, 1986	The Salk Institute, La Jolla, California.
April, 1986	Symposium on Suppression of Carcinogenesis, FASEB St. Louis, Missouri.
April, 1986	Current Topics Lecture, Radiation Research Society of North America, Las Vegas, Nevada.
May, 1986	Frederick Cancer Research Center, Frederick, Maryland.
May, 1986	Symposium on Cancer Biology, American Association for Cancer Research, Los Angeles, California.
May, 1986	The Wistar Institute, Philadelphia, Pennsylvania.
May, 1986	Symposium on Growth Factors, Oncogenes and Cancer, American Association for the Advancement of Science, Philadelphia, Pennsylvania.
May, 1986	Symposium on Quantitative Biology: Molecular Biology of Homo Sapiens, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York.
June, 1986	Symposium on Cancer Genetics, Genetics Society of America, Champaign-Urbana, Illinois.
August, 1986	Symposium on Oncogenes, Symposium on Cancer Genetics, 14th International Cancer Congress, Budapest, Hungary.
August, 1986	Biological Research Center, Hungarian Academy of Sciences, Szeged, Hungary.
September, 1986	Nature Conference, "Exploring the Human Genome", Boston, Massachusetts.
October, 1986	Frederick Cancer Research Center, Frederick, Maryland.
November, 1986	Chair, Session on Ras-related Genes, Princess Takamatsu Symposium on Cancer Research, Tokyo, Japan.
November, 1986	Chair, Symposium on the Somatic Cell Genetics of Cancer, American Society for Human Genetics, Philadelphia, Pennsylvania.
November, 1986	Department of Biology and the Cancer Center, Massachusetts Institute of Technology, Cambridge, Massachusetts.
January, 1987	Lady Davis Research Institute, Jewish General Hospital, Montreal, Canada.
January, 1987	Departments of Biology and Human Genetics, Queen's University, Kingston, Canada.
February, 1987	American Association for the Advancement of Science Symposium on Chromosome Abnormalities in Human Cancer: Biological and Diagnostic Implications, Chicago, Illinois.
March, 1987	Department of Medical Genetics, Hospital for Sick Children, Toronto, Canada.
March, 1987	Frontiers in Biological Sciences Lecture Case Western Reserve University, Cleveland, Ohio.
April, 1987	Director's Seminar, National Cancer Institute, Washington, D.C.
May, 1987	International Conference on Progress in Cancer Research, San Remo, Italy.
May, 1987	Department of Human Genetics, University of Manitoba, Winnipeg, Canada.
June, 1987	Symposium on Molecular Biology and Medicine, Canadian Society of Laboratory Medicine, Quebec City, Canada.
June, 1987	Molecular Neurobiology of Human Disease, Cold Spring Harbor, New York.
June, 1987	Canadian Congress of Ophthalmology, Montreal, Canada.
July, 1987	Chair, Session on New Oncogenes, Frederick Oncogene Meeting, Frederick, Maryland.
July, 1987	FASEB Conference on Mechanisms of Carcinogenesis, Saxton's River, Vermont.
July, 1987	Gordon Conference on Chemotherapy of Experimental and Clinical Cancer, New London, New Hampshire.
September, 1987	Symposium on Growth Factors and Oncogenes, Royal Swedish Academy of Sciences, Uppsala, Sweden.
September, 1987	Department of Virology, University of Helsinki, Finland.

September, 1987	International Union Against Cancer Symposium of Growth Factors and Oncogenes, Hole, Massachusetts.
October, 1987	Fullbright Lectures, University of Siena Medical School Italy.
November, 1987	M.D. Anderson Symposium on Fundamental Cancer Research, Houston, Texas.
November, 1987	The Wistar Institute, Philadelphia, Pennsylvania.
November, 1987	Memorial University Medical School, St. John's, Newfoundland.
January, 1988	Symposium on Genetic Medicine, University of Texas Health Sciences Center - Dallas.
February, 1988	United States - Japan International Meeting on Oncogenes. Kauai, Hawaii.
March, 1988	Preuss Foundation Symposium on Brain Tumors, San Diego, California.
March, 1988	Department of Biochemistry, University of California San Francisco, California.
April, 1988	Department of Pathology, Stanford University School of Medicine, California.
April, 1988	Abbott Laboratories, Chicago, Illinois.
April, 1988	Institute for Human Genetics, University of Minnesota Medical School, Minneapolis, Minnesota.
May, 1988	Collaborative Research, Boston, Massachusetts.
May, 1988	Cancer Center, University of North Carolina, Chapel Hill, North Carolina.
May, 1988	National Institute of Environmental Health Science, Research Triangle Park, North Carolina.
May, 1988	Department of Pathology, University of Vermont School of Medicine, Burlington, Vermont.
May, 1988	Chair, Symposium on Tumor Suppressors, American Association for Cancer Research, New Orleans, Louisiana.
June, 1988	Fred Hutchinson Cancer Center, Seattle, Washington.
July, 1988	Chair, Session on Oncogenes, FASEB Conference on Molecular and Cellular Biology, Saxton's River, Vermont.
July, 1988	Ciba Foundation Symposium, London, England.
August, 1988	Gordon Conference on Cancer, Newport, Rhode Island.
August, 1988	Symposium on Oncogenetics, International Congress on Genetics, Toronto, Canada.
September, 1988	Department of Biochemistry, State University of New York, Stony Brook, New York.
October, 1988	Bristol-Myers Symposium, Madison, Wisconsin.
October, 1988	Club de recherches cliniques du Quebec, Pointe au Pic, Quebec.
October, 1988	Pediatric Ophthalmology Conference, Montreal, Quebec.
December, 1988	University of Washington, School of Medicine, St. Louis, Missouri.
December, 1988	American Society of Hematology, San Antonio, Texas.
January, 1989	Arnold O. Beckman Conference, Ft. Lauderdale, Florida.
January, 1989	Department of Pathology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.
February, 1989	Pathogenesis and Prevention of Hepatocellular Carcinoma, Honolulu, Hawaii.
February 1989	St. Jude's Children's Research Hospital, Memphis, Tennessee.
February, 1989	Arizona Cancer Center, Tucson, Arizona.
March, 1989	FASEB, New Orleans, Louisiana.
March 1989	University of Rochester, Rochester, New York.
March, 1989	Organizer, Banbury Conference on Recessive Oncogenes, Cold Spring Harbor, NY.
March 1989	University of Colorado, Denver, Colorado.
April, 1989	College of Physicians and Surgeons, Columbia University, New York, New York.
April, 1989	University of Utah, Salt Lake City, Utah.
April, 1989	American Association of Neurological Surgeons, Washington, D.C.
May, 1989	NATO-ASI Meeting, Mallorca, Spain.
May, 1989	Genetics in Cancer and Development, Groningen, The Netherlands.
June, 1989	American Association for Cancer Research, San Francisco, California.
June, 1989	American Association of Neuropathologists, Dallas, Texas.
June, 1989	Endocrine Society, Seattle, Washington.

June 1989	America Society of Hematology, San Diego, California.
July, 1989	Gordon Conference on Hormonal Carcinogenesis, New Hampton, New Hampshire.
August, 1989	FASEB on Molecular Mechanisms of Carcinogenesis, Copper Mountain, Colorado.
August, 1989	Gordon Conference on Cancer, Newport, Rhode Island.
September, 1989	Berzelius Symposium 27th: Molecular Genetics and Human Diseases, Uppsala, Sweden.
September, 1989	International Symposium on Brain Tumors, Zermatt Switzerland.
September, 1989	Usha Symposium, University of California, San Diego.
September, 1989	Bristol Myers Symposium, Toronto, Canada.
September, 1989	UICC Symposium, Woods Hole, Massachusetts.
November, 1989	General Motors Foundation Lecture, New York City.
November, 1989	International Symposium on Rhabdomyosarcoma, Columbus, Ohio.
November, 1989	Princess Takamatsu Symposium, Tokyo, Japan.
November, 1989	Mildred Scheel Symposium, Bonn, West Germany.
November, 1989	University of Oxford, United Kingdom.
December, 1989	University of Southern California Symposium, Los Angeles, California.
December, 1989	University of Chicago Cancer Center.
January, 1990	US/Japan meeting on Cancer Genes, Kauai, Hawaii.
February, 1990	Preuss Foundation for Brain Tumor Research, La Jolla, California.
February, 1990	London Neurosciences Center, London, Ontario.
March, 1990	FASEB Conference on Growth Suppressors, Taos, New Mexico.
March, 1990	Metpath, Inc. Paterson, New Jersey.
March, 1990	Symposium on Cancer Suppressors, University of North Carolina, Chapel Hill.
April, 1990	Cleveland Clinic, Cleveland, Ohio.
April, 1990	Department of Human Genetics, University of Pennsylvania, Philadelphia.
May, 1990	Symposium on Childhood Malignancies, Stockholm, Sweden.
May, 1990	NATO/ASI course on Cancer Genes, Erice, Sicily.
June, 1990	Steele Symposium on Developmental Oncology, New York City.
June, 1990	Division of Pediatric Oncology, Dana Farber Cancer Center, Boston.
July, 1990	European Workshop on Cytogenetics and Molecular Genetics of Solid Tumors, Leuven, Belgium.
August, 1990	Gordon Conference on Cancer, Newport, Rhode Island.
September, 1990	Symposium on Origins of Human Cancer, Cold Spring Harbor, New York.
September. 1990	Department of Biology, Princeton University.
October, 1990	Department of Biochemistry and Biophysics, University of Pennsylvania, Philadelphia.
October, 1990	Symposium on Bladder Cancer, Prout's Neck, Maine.
October, 1990	Symposium on Pediatric Tumors, Milan, Italy.
November, 1990	Department of Human Genetics, University of Minnesota, Minneapolis.
January, 1991	Miami Winter Symposium.
February, 1991	Symposium on Developmental Tumors, American Association for Cancer Research, San Diego.
February, 1991	Australian Research Society, Melbourne.
March, 1991	Institute of Medicine, Washington, D.C.
March, 1991	Medical College of Virginia, Richmond.
April, 1991	Lasker Symposium, ACS, Sarasota, Florida.
April, 1991	Environmental Mutagen Society, Orlando, Florida.
April, 1991	McMaster University, Hamilton, Ontario.
April, 1991	ACS Symposium, Miami, Florida.
April, 1991	Max Planck Symposium on Glioma, Goslar, West Germany.
April, 1991	Ares-Serono Symposium on Heritable Tumors, Florence, Italy.
May, 1991	Symposium on Tumor Progression, Association for Cancer Research, Houston, Texas.
June, 1991	Rush Symposium, Chicago, Illinois.
July, 1991	Radiation Research Congress, Toronto, Ontario.

September, 1991	Usha Mahajani Symposium, University of California, San Diego.
September, 1991	150 Anniversary Symposium Belgian Academy of Sciences, Brussels, Belgium.
October, 1991	AACR Symposium on Growth Regulators, Chatham, Massachusetts.
October, 1991	44th Symposium on Fundamental Cancer Research, Houston, Texas.
January, 1992	American Red Cross, Washington, D.C.
February, 1992	Keystone Symposium on Neural Crest, Taos, New Mexico.
February, 1992	University of Kansas, Kansas City.
April, 1992	Symposium on Oncogenes, Madrid, Spain.
June, 1992	City of Hope, Duarte, California.
July, 1992	Chair, Symposium on Tumor Suppressors, International Congress of Cell Biology, Madrid, Spain.
September, 1992	Harris Symposium, Oxford, UK.
October, 1992	Bristol Myers-Squibb Research Institute, Princeton, New Jersey.
October, 1992	Steel Symposium on Pediatric Brain Tumors, New York.
October, 1992	AACR Symposium on Cancer and Differentiation, Chatham, Massachusetts.
November, 1992	Symposium on Oncogenes, Rome, Italy.
November, 1992	Cancer Center, Yale University, New Haven, Connecticut.
January, 1993	Cancer Center, University of California-Irvine.
February, 1993	Symposium on Childhood Cancer, Sydney, Australia.
March, 1993	Symposium on Cofactors in Cancer, Nice, France.
March, 1993	Canji Corporation, La Jolla, California.
March, 1993	Merck, West Point, Pennsylvania.
April, 1993	Fogarty Symposium on Human Disease, Washington, D.C.
May, 1993	Symposium of Molecular Genetics, American Association of Neurological Surgeons, San Diego, California.
July, 1993	Aspen Symposium, Colorado.
August, 1993	Chair, Session on Tumor Suppressors, International Congress of Genetics, Birmingham, UK.
August, 1993	Chair, Session on Cancer Genetics, Gordon Conference on Molecular Genetics, Newport, Rhode Island.
September, 1993	Symposium on Cancer Biology, Camargo Hospital, Sao Paulo, Brazil.
September, 1993	Symposium on AIDS and Cancer, Loutraki, Greece.
October, 1993	Course "Review Neurology and Neurosurgery", Woods Hole, Massachusetts.
October, 1993	Beatson Institute, Glasgow, Scotland, UK.
December, 1993	Symposium on "Medicine in the 21st Century", Yokohama, Japan.
December, 1993	Karolinska Institute, Stockholm, Sweden.
April, 1994	Bristol Myers Symposium on Cancer, Segovia, Spain.
April, 1994	Symposium on Tumor Suppressors, FASEB, AAP, Anaheim, California.
October, 1994	Symposium on Molecular Biology, International Society of Child Neurology, San Francisco, California.
October, 1994	Symposium on Molecular Neuro-Oncology, International Congress of Neurosurgeons, Chicago, Illinois.
November, 1994	Chair, Symposium on Tumor Suppressor, UICC Congress, New Delhi, India.
November, 1994	Symposium on Cancer, International Society of Pathophysiology, Kyoto, Japan.
November, 1994	National Cancer Center Research Institute, Tokyo Japan.
December, 1994	Fred Hutchinson Cancer Center Symposium on Glioblastoma, Seattle, Washington.
December, 1994	Symposium on Tumor Suppressors, Children's Hospital of Los Angeles.
January, 1995	40th Anniversary Symposium, UMDNJ, Newark, New Jersey.
February, 1995	Chair, Symposium on Tumor Progression, AACR/JACR Congress, Maui, Hawaii.
April, 1995	Henry Ford Hospital, Detroit, Michigan.
May, 1995	University of California, Los Angeles.
July, 1995	Institute of Cell Biology, Essen, Germany.
August, 1995	M.D. Anderson Institute, Houston, Texas.
August, 1995	John Wayne Cancer Center, Santa Monica, California.

September 1995	International Symposium on Pathobiology, Alicante, Spain.
October, 1995	Corning Clinical Labs, Teterboro, New Jersey.
November, 1995	Princess Takamatsu Cancer Symposium, Tokyo, Japan.
November, 1995	Brain Tumor Symposium, Wistar Institute, Philadelphia, Pennsylvania.
January, 1996	Symposium on Cancer Genetics, Children's Hospital of Los Angeles, California.
February, 1996	Grand Rounds, Roswell Park Memorial Cancer Institute, Buffalo, New York.
March, 1996	Banyu Research Institute, Tsukuba, Japan.
April, 1996	Dept. of Anatomy and Cell Biology, University of Cincinnati, Ohio.
April, 1996	Symposium on Angiogenesis, Annual Meeting of the AACR, Washington, DC.
May, 1996	Short Course in Cancer Biology, Eppley Research Institute, Omaha, Nebraska.
May, 1996	Symposium on Brain Tumor Genetics, American Society of Child Neurology, Washington, DC.
June, 1996	Symposium on Tumor Suppressors, American Society of Investigative Pathology, New Orleans, Louisiana.
June, 1996	NATO-ASI Course on Cancer Biology, Elba, Italy.
July, 1996	Aspen Cancer Conference, Aspen, Colorado.
October, 1996	Chair, Session on Neuro-Oncology, International Symposium on Diseases of the Central Nervous System, Bonn, Germany.
January, 1997	University of North Carolina Cancer Center, Chapel Hill, North Carolina.
March, 1997	40th Annual Clinical Conference, M D Anderson Cancer Center, Houston, Texas.
March, 1997	Inaugural Symposium, University of California Cancer Center, San Francisco, California.
May, 1997	St. Jude Hospital, Memphis, Tennessee.
June, 1997	Chair, Plenary Session on Cancer, Molecular Medicine Society, San Diego, California.
July, 1997	Aspen Cancer Conference, Aspen, Colorado.
August, 1997	Symposium on Cancer, International Congress of Biochemistry and Molecular Biology, San Francisco, CA.
September, 1997	3rd International Conference on Gene Regulation/Oncogenesis/Aids. Spetsai, Greece.
September, 1997	FASEB Symposium on Tumor Biology, San Francisco, California.
October, 1997	Basic Science Symposium, M D Anderson Cancer Center, Houston, Texas.
November, 1997	Princess Takamatsu Cancer Symposium, Tokyo, Japan.
November, 1997	7th International Symposium of the Hiroshima Cancer Seminar, Hiroshima, Japan.
February, 1998	Preuss Foundation Symposium, San Diego California.
March, 1998	Smith Kline-Beecham Symposium on Genomics, Melbourne, Australia.
May, 1998	Case Western Reserve University, Cleveland, Ohio.
June, 1998	Istituto Regina Elena, Rome, Italy.
June, 1998	International Symposium on Melanoma, Istituto Dermopatico Dell'Immacolata, Rome, Italy.
July, 1998	Aspen Cancer Conference, Aspen, Colorado.
October, 1998	Weiss Center, Pennsylvania State University, Danville, Pennsylvania.
October, 1998	3rd World Congress on Cancer, Crete, Greece.
October, 1998	Symposium on Receptor Signalling, International Union of Biochemistry and Molecular Biology, Jerusalem, Israel.
October, 1998	Plenary Symposium, American Society of Therapeutic and Radiation Oncology, Phoenix, Arizona.
April, 1999	Chair, Symposium on Late-Breaking Results, Annual Meeting of the American Association for Cancer Research, Philadelphia, Pennsylvania.
May, 1999	Grand Rounds, Dept. of Neurosurgery, University of California-Los Angeles.
May, 1999	International Symposium on Molecular Oncology, Positano, Italy.
June, 1999	25th Anniversary Symposium of the Cancer Center, Massachusetts Institute of Technology, Cambridge, Massachusetts.

September, 1999	58th Annual Meeting of the Japanese Cancer Association, Hiroshima, Japan.
October, 1999	44th Annual Meeting, German Association for Neuropathology and Neuroanatomy and the Swiss Society for Neuropathology, Bonn, Germany.
November, 1999	International Symposium on Cancer Prevention and Treatment, Beijing, China.
November, 1999	14th Annual The San Diego Conference, the American Association for Clinical Chemistry, San Diego, CA.
May, 2000	National Cancer Center Research Institute, Tokyo, Japan.
May, 2000	Chair, Symposium on Molecular Biology of Gliomas, 18th Annual Meeting of the Japan Society of Brain Tumor Pathology, Nagoya, Japan.
May, 2000	Special Seminar on Pathology and Genetics of Tumors of the Nervous System, 18th Annual Meeting of the Japan Society of Brain Tumor Pathology, Nagoya, Japan.
July, 2000	Aspen Cancer Conference, Aspen, CO.
August, 2000	West Coast Conference on Genomics, Lawrence Berkeley National Laboratory, Berkeley.
September, 2000	Vatican Conference on Biology, Rome, Italy.
March, 2001	Environmental Mutagen Society, San Diego, CA.
April, 2001	Cancer Center, University of California-San Francisco.
July, 2001	Aspen Cancer Conference, Aspen, CO.
February, 2002	Chair, Symposium on "New Targets in Cancer Therapy", 12th International Congress on Anti-Cancer Treatment, Paris, France.
February, 2002	Novartis Genome Research Institute, San Diego, CA.
March, 2002	Vogt Symposium, Scripps Research Institute, San Diego, CA.
April, 2002	CNRC-NRC Biotechnology Research Institute, Montreal, Canada.
April, 2002	Cancer Center, Duke University, Durham, NC.
May, 2002	CLINBIO-2002, Capri, Italy.
July, 2002	Aspen Cancer Conference, Aspen, CO.
September, 2002	UCSF Brain Tumor Symposium, San Francisco, CA.
September, 2002	The Neurosciences Summit, La Jolla, CA.

Molecular Mechanisms of Apoptosis Regulation

A tumor-specific mutant epidermal growth factor receptor confers cisplatin resistance in human glioblastoma cells by modulating Bcl-XL and caspase-3. Motoo Nagane, Webster K. Cavenee, H-J. Su Huang. Ludwig Institute for Cancer Research, La Jolla, CA 92093-0660, U.S.A.

Alterations of epidermal growth factor receptor (EGFR) occur frequently in gliomas and are restricted to highly malignant glioblastomas. The most common alteration is deletion of exon 2-7 resulting in the mutant receptor with truncation in its extracellular domain (ΔEGFR). Introduction of ΔEGFR into human glioma U87MG cells (U87MG.ΔEGFR) resulted in expression of constitutively kinase-activated ΔEGFR on the cell membrane and conferred remarkably enhanced tumorigenicity, while a kinase-deficient mutation (DK) of ΔEGFR almost abolished this potential. This enhanced tumorigenicity by ΔEGFR was mediated by an increase in proliferation and also a decrease in apoptosis of tumor cells. Among apoptosis-related genes, expression of Bcl-XL, an apoptosis inhibitor, was upregulated in U87MG.ΔEGFR tumors, which was inversely correlated with the reduced apoptotic rate. These data suggested that ΔEGFR may play an important role as a survival factor in tumor cells. To test this hypothesis, we investigated the sensitivity of cells to a chemotherapeutic drug, cisplatin (CDDP), a DNA damaging agent which is known to induce apoptosis. By colony forming efficiency assays, the IC_{50} value of U87MG.ΔEGFR cells to CDDP was 11.3 μg/ml, 4-fold higher than those of parental U87MG (2.8) and U87MG.DK (2.7) cells. This CDDP resistance in U87MG.ΔEGFR cells was inversely correlated with a reduced apoptotic rate after CDDP treatment (~5-fold less than U87MG and U87MG.DK cells) measured by TUNEL assays. Similar findings were observed by Annexin V binding assays. Caspase-3 (CPP32) activity increased in U87MG and U87MG.DK cells after CDDP treatment which could be inhibited by incubation with both caspase inhibitors, z-Asp-CH_2-DCB in cell culture and Ac-DEVD-CHO in cell lysates. In contrast, caspase-3 activation was 2- to 3-fold lower in U87MG.ΔEGFR cells. Consistent with this observation, cleavage of PARP, a cellular substrate of caspase-3, was dramatically enhanced 48 h after CDDP treatment in U87MG and U87MG.DK cells, whereas it was at trace level in U87MG.ΔEGFR cells. Moreover, the induction of apoptosis by CDDP in U87MG and U87MG.DK cells could be abolished by treatment of the caspase inhibitor z-Asp-CH_2-DCB. To determine the role of Bcl-XL overexpression in U87MG.ΔEGFR in CDDP resistance, U87MG cells were transfected with either a Bcl-XL expression vector, pSFFV/Bcl-XL, or control vector, pSFFV, and stable clones with various levels of Bcl-XL overexpression were established following G418 selection. As expected, U87MG.Bcl-XL clones (-6, 9, 13) with high expression of Bcl-XL exhibited the lowest apoptosis rate and caspase-3 activity after CDDP treatment. U87MG.Bcl-XL-11, a clone with similar Bcl-XL expression level to that of U87MG.ΔEGFR cells, showed a moderate apoptotic rate reduction and caspase-3 activation, which were similar to those of U87MG.ΔEGFR cells. Control vector transfectants (U87MG.SFFV) did not demonstrate inhibition of apoptosis or caspase activation. Our results are consistent with the prediction that ΔEGFR transduces signals for tumor cell survival and that this is mediated, at least in part, through overexpression of Bcl-XL in glioblastoma cells. In this regard, ΔEGFR could be a potential target in glioblastoma cells expressing this molecule in glioma therapy. To explore this possibility, we are currently testing CDDP treatment of U87MG.ΔEGFR cells in combination with tyrphostins, specific tyrosine kinase inhibitors of ΔEGFR, and the results will be presented.